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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,522	12/13/2000	Seishi Kato	GIN-6714CPUS	7220

7590 06/17/2003

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EXAMINER
WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,522	KATO ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-16* is/are pending in the application.

4a) Of the above claim(s) *13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-12 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/13/00* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendments filed 30 September 2002 (Paper No. 10) and 21 January 2003 have been entered. Claims 1-6 are canceled. Claim 16 was added in paper 10 and reads on the elected Invention. Applicant has requested clarification on election of the Sequence for the instant Application (30 September 2002, Paper No. 10, page 4). Applicant elected SEQ ID NO: 4, without traverse, in Paper 8 (12 February 2002, page 3).

Claims 7-12 and 16 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

Title

The objection to the title as set forth at p. 3 of the previous Office Action (Paper No. 9, 22 April, 2002, page3) is *withdrawn* in view of the amendment which introduced a new title (Paper No. 10, 30 September 2002).

Filing History

The objection to the Specification for not listing Continuity Data in the first paragraph of the Specification, as set forth at p. 3 of the previous Office Action (Paper No. 9, 22 April, 2002,

page3) is *withdrawn* in view of the amendment which introduced priority data in the first paragraph of the Specification (Paper No. 10, 30 September 2002).

Title

The objection to the Specification for lacking an Abstract, as set forth at p. 4 of the previous Office Action (Paper No. 9, 22 April, 2002, page3) is *withdrawn* in view of the amendment which introduced an Abstract (Paper No. 10, 30 September 2002).

Maintained Objections and/or Rejections

Sequence Rules

As set forth in the previous Office Action (Paper 9, 22 April 2002, pages 3-4), the instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules must be accompanied by the required reference to the (one) relevant sequence identifier (i.e., SEQ ID NO:). Each sequence must be followed by the particular SEQ ID NO: assigned to that sequence. For example, there are not three SEQ ID NO:'s for each disclosed sequence as listed in Figures 1-7.

Appropriate correction is required.

35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.

Claims 7-12 and 16 are rejected under 35 U.S.C. 101, as lacking utility. The reasons for this rejection under *35 U.S.C. § 101* are set forth at pp. 4-11 of the previous Office Action (Paper

No. 9, 22 April 2002). Claims 7-12 and 16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (Paper No. 9, 22 April 2002), one skilled in the art clearly would not know how to use the claimed invention.

The claims are directed to a protein that possesses approximately 80- 93% homology to known proteins, such as FK506-binding protein (93%) (Guan, et al, 1999, Accession No. Q9Y680) and Human Cornichon-like protein (80%) (Utku, et al, 2003, Accession No. NP_005767). A large central portion of the polypeptide of SEQ ID NO: 4 – specifically amino acids 26-122 – bears 99% homology to mouse Cornichon protein. As discussed in the previous Office Action (p. 5), no well-established utility exists for newly isolated complex biological molecules. The specification does not disclose experiments that impart *any* function for the claimed polypeptide in the context of the cell or organism. The specification does not teach the skilled artisan how to use the peptide for any unique or specific purpose. For example, there are no data disclosed in which cells undergo morphogenic changes when transfected with a gene encoding SEQ ID NO: 4. Neither are there experiments that demonstrate precisely *which* morphogenic changes can be expected in cells expressing or responding to the polypeptide of SEQ ID NO: 4. The skilled artisan is not provided with sufficient guidance to use the claimed polypeptide for any specific purpose.

Applicants argue (page 5 and throughout, Paper No. 10, 30 September, 2002) that the peptide disclosed in the instant Specification is a Cornichon protein, and that homology of the disclosed polypeptide with a class of proteins *already having* utility shall impart sufficient utility

on the novel polypeptide and on the polynucleotide(s) encoding it. The instant Specification states that Cornichon-like proteins (See, for example: Utku, et al, 2003, Accession No. NP_005767) are important in *morphogenesis* (page 49).

Applicant's arguments have been fully considered but they are not persuasive for the following reasons:

Without specific functional assays, the polypeptide of the Instant Specification and the polynucleotide encoding are unidentified molecules. The disclosed polypeptide bears significant (80-93%) homology to EF-hand proteins, such as Cornichon. However, aside from homology, very little information is given in the Specification about an identifying unique or specific function for the claimed polypeptide of SEQ ID NO: 4.

Applicants further argue (page 5 Paper No. 10, 30 September, 2002) that the claims were rejected under 35 U.S.C § 101, for not having a utility that is *credible*. Applicant's arguments have been fully considered but they are not persuasive for the following reasons:

The examiner has not discussed the credibility of the utility claims, only the lack of a *specific* and *substantial* utility for the claimed polypeptide. In fact claims of function for a new polypeptide are generally deemed "credible" unless they violate laws of nature (Federal Register, 2001, 66: 4, p. 1098). The examiner agrees that the asserted utility for the claimed polypeptide is possible within the laws of nature.

Applicants argue (page 6 Paper No. 10, 30 September, 2002) that the art does not support the contention that function of a polypeptide cannot be deduced from homology to other known sequences, citing:

"[h]omologous proteins result from speciation or differentiation. Comparisons between homologous proteins have yielded general rules for protein structures... In this context it is often useful to distinguish between protein speciation and protein differentiation... Speciation is the evolution of homologous proteins possessing a common function in different organisms" (*Principles of Protein Structure*, Cantor, ed., 1978, page 167).

Applicant's arguments have been fully considered but they are not persuasive for the following reasons:

The above reference is not relevant to a discussion of ascribing a specific function to a new polypeptide. In fact the author states that "comparisons between homologous proteins have yielded *general* rules for protein structures." The examiner agrees with this position. There certainly *are* general statements that can be made about protein structures as related to function. For example, the transmembrane domains of many receptor proteins are alpha helices comprised of hydrophobic amino acids. The fact that this is true for a wide variety of receptors says nothing at all about each receptor's specific function within the organism, only that the hydrophobic alpha helix is evolutionarily the "best" structure for traversing a cell's plasma membrane.

The applicant further cites (page 6 Paper No. 10, 30 September, 2002) a reference as evidence that "establishing homology between the unknown and reference proteins permits the skilled artisan to assume the unknown unexpressed protein and the known reference protein have the same function" (Hieter, P and Boguski, M., 1997, Science, 278: 5338: 601-602). This Letter or Comment to Science discusses the term "Functional Genomics". It does not express an opinion on the problem of inferring function from protein homology, except to remark that:

"In the past we have had functions in search of sequences. In the future, pathology and physiology will become 'functionators' for the sequences" (p. 601, paragraph 6).

To paraphrase then: In the future, sequences will be in search of pathologies and physiologies, not the other way around. This is an interesting point of the article, but not particularly relevant to a discussion of inferring function from homology, and is certainly not probative of the applicant's statement that: "establishing homology between the unknown and reference proteins permits the skilled artisan to assume the unknown unexpressed protein and the known reference protein have the same function" (page 6 Paper No. 10, 30 September, 2002).

Applicants cite (page 6 Paper No. 10, 30 September, 2002) a letter sent from the president of the American Society of Human Genetics, Ronald Worton, to commissioner Dickinson, dated 22 March 2000. The examiner has not been able to locate a copy of this letter, but private correspondence from partisan individuals would not generally be considered good supporting evidence for the contention that "establishing homology between the unknown and reference proteins permits the skilled artisan to assume the unknown unexpressed protein and the known reference protein have the same function" (page 6 Paper No. 10, 30 September, 2002).

Likewise, the examiner has not been able to locate the "Utility Training Materials" referred to by the Applicant (page 6 Paper No. 10, 30 September, 2002). Copies of both the Letter referred to above and the "Utility Training Materials" is requested.

Applicants state (page 7, Paper No. 10, 30 September, 2002) that the "PTO acknowledges as well utility is well-established if it is readily apparent to one skilled in the art" and cites the case of Enzo Biochem. v Gen-Probe (Appeal No. 01-1230, Federal Circuit).

Applicant's arguments have been fully considered but they are not persuasive for the following reasons:

In fact the "Enzo" case concerned the "Written Description" requirements of a nucleic acid. In the Appeal it was decided that reference in the patent Specification to a deposit of genetic material may suffice to describe that material. The case makes no reference or discussion to the *function* of biological material based on homology. In the instant Application, the Written Description requirement has been satisfied by disclosure of the entire sequence of the claimed polypeptide (SEQ ID NO: 4).

Applicants further discuss *In re Folkers* (1965, 145 USPQ 390) in terms of assigning function to a new protein (pages 7-8, Paper No. 10, 30 September, 2002). However, the fact patterns of that case are substantially different than the current Application and in fact are more important to discussions of a protein having a "well-established" Utility. The "Folkers" case requires the examiner to first ascertain if there is a well-established utility for the claimed polypeptide or polynucleotide. The example given in the case is that of insulin. Its utility would not have to be demonstrated by an applicant claiming that exact polypeptide, since the function of insulin is well-established.

Applicants point out (page 8, Paper No. 10, 30 September, 2002) that the "present invention can be further utilized as research tools for better characterizing the prior art mouse Cornichon compound."

Despite the Applicant's arguments, the Patent Office makes clear that the usefulness of new polypeptides does not include "entry point" and speculative experiments (Federal Register, 2001, 66 (4): p. 1094). There is no evidence that the protein disclosed in the instant

Specification functions like *Cornichon*, an EF-hand protein or as a morphogenic protein. However, even if it were established as such, additional specific functional assays would be needed since, even though research on these proteins is in the early stages, members of this family of proteins no doubt have a variety of functions, such as establishing "egg asymmetry" (Powers, et al, 1998, J. Cell Biol., 142(5): 1209-1222), or "Isomerase" (Guan, et al, 1999, Accession No. Q9Y680) or "alloactivation of T-cells" (Utku, et al, 2003, Accession No. NP_005767). Therefore, one skilled in the art would not know the utility and function of the polypeptide disclosed in the instant application, even if it *were* established as a Cornichon protein.

Furthermore, the discussions above concerning the function of the polypeptide of SEQ ID NO: 4 also apply to the claimed fragments of SEQ ID NO: 4. It has not been shown that the full-length polypeptide functions in "morphogenesis", or what specific morphogenetic function is being referred to; therefore, the same issues are also relevant to short fragments of the polypeptide of SEQ ID NO: 4.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine the function of the protein of SEQ ID NO: 4, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of predicting the function of new proteins based on structure, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

New Objections/Rejections

Claim 16 is objected to for reciting non-elected inventions (SEQ ID NO: 11 and 21).

Conclusion

No claims are allowed. Claim 16 is objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

13 June 2003

GARY KUNZ
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